pharmacology, endocrinology, or related fields are intended to be within the scope of the invention.

What is claimed is:

Claims

1. A composition comprising a non-steroidal immunophilin-dependent immunosuppressant (NsIDI) and an NsIDI enhancer (NsIDIE) in amounts that together are sufficient *in vivo* to decrease proinflammatory cytokine secretion or production or to treat an immunoinflammatory disorder.

2. The composition of claim 1, wherein said NsIDI is a calcineurin inhibitor.

3. The composition of claim 2, wherein said calcineurin inhibitor is cyclosporine, tacrolimus, ascomycin, pimecrolimus, or ISAtx247.

4. The composition of claim 1, wherein said said NsIDI is an FK506-binding protein.

5. The composition of claim 4, wherein said FK506-binding protein is rapamycin or everolimus.

6. The composition of claim 1, wherein said NsIDIE is a selective serotonin reuptake inhibitor (SSRI), a tricyclic antidepressant (TCA), a phenoxy phenol, an antihistamine, a phenothiazine, or a mu opioid receptor agonist.

7. The composition of claim 6, wherein said SSRI is selected from the group consisting of fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram, and escitalopram.

8. The composition of claim 6, wherein said TCA is selected from the group consisting of maprotiline, nortriptyline, protriptyline, desipramine,

amitriptyline, amoxapine, clomipramine, dothiepin, doxepin, desipramine, imipramine, lofepramine, mianserin, oxaprotiline, octriptyline, and trimipramine.

9. The composition of claim 6, wherein said phenoxy phenol is triclosan.

10. The composition of claim 6, wherein said antihistamine is selected from the group consisting of ethanolamines, ethylenediamines, phenothiazines, alkylamines, piperazines, piperidines, and atypical antihistamines.

11. The composition of claim 6, wherein said antihistamine is selected from the group consisting of desloratadine, thiethylperazine, bromodiphenhydramine, promethazine, cyproheptadine, loratadine, clemizole, azatadine, cetirizine, chlorpheniramine, dimenhydramine, diphenydramine, doxylamine, fexofenadine, meclizine, pyrilamine, and tripelennamine.

12. The composition of claim 6, wherein said phenothiazine is chlorpromazine or ethopropazine.

13. The composition of claim 6, wherein said mu opioid receptor agonist is a piperidine butyramide derivative.

14. The composition of claim 6, wherein said mu opioid receptor agonist is loperamide, meperidine, or diphenoxylate.

15. The composition of claim 1, wherein said composition further comprises a non-steroidal anti-inflammatory drug (NSAID), COX-2 inhibitor, biologic, small molecule immunomodulator, disease-modifying anti-rheumatic drugs (DMARD), xanthine, anticholinergic compound, beta receptor agonist,

bronchodilator, non-steroidal calcineurin inhibitor, vitamin D analog, psoralen, retinoid, or 5-amino salicylic acid.

16. The composition of claim 15, wherein said NSAID is ibuprofen, diclofenac, or naproxen.

17. The composition of claim 15, wherein said COX-2 inhibitor is rofecoxib, celecoxib, valdecoxib, or lumiracoxib.

18. The composition of claim 15, wherein said biologic is adelimumab, etanercept, or infliximab.

19. The composition of claim 15, wherein said DMARD is methotrexate or leflunomide.

20. The composition of claim 15, wherein said xanthine is theophylline.

21. The composition of claim 15, wherein said anticholinergic compound is ipratropium or tiotropium.

22. The composition of claim 15, wherein said beta receptor agonist is ibuterol sulfate, bitolterol mesylate, epinephrine, formoterol fumarate, isoproteronol, levalbuterol hydrochloride, metaproterenol sulfate, pirbuterol scetate, salmeterol xinafoate, or terbutaline.

23. The composition of claim 15, wherein said vitamin D analog is calcipotriene or calcipotriol.

24. The composition of claim 15, wherein said psoralen is methoxsalen.

25. The composition of claim 15, wherein said retinoid is acitretin or tazoretene.

26. The composition of claim 15, wherein said 5-amino salicylic acid is mesalamine, sulfasalazine, balsalazide disodium, or olsalazine sodium.

27. The composition of claim 15, wherein said small molecule immunomodulator is VX 702, SCIO 469, doramapimod, RO 30201195, SCIO 323, DPC 333, pranalcasan, mycophenolate, or merimepodib.

28. The composition of claim 1, wherein said composition is formulated for topical administration.

29. The composition of claim 1, wherein said composition is formulated for systemic administration.

30. A method of decreasing proinflammatory cytokine secretion or production in a patient, said method comprising administering to the patient an NsIDI and an NsIDIE simultaneously or within 14 days of each other in amounts sufficient *in vivo* to decrease proinflammatory cytokine secretion or production in said patient.

31. A method for treating a patient diagnosed with or at risk of developing an immunoinflammatory disorder, said method comprising administering to the patient an NsIDI and an NsIDIE simultaneously or within 14 days of each other in amounts sufficient to treat said patient.

32. The method of claim 31, wherein said immunoinflammatory disorder is rheumatoid arthritis, Crohn's disease, ulcerative colitis, asthma, chronic obstructive pulmonary disease, polymylagia rheumatica, giant cell arteritis, systemic lupus erythematosus, atopic dermatitis, multiple sclerosis, myasthenia gravis, psoriasis, ankylosing spondylitis, or psoriatic arthritis.

33. The method of claim 31, wherein said NsIDI is cyclosporine, tacrolimus, ISAtx247, ascomycin, pimecrolimus, rapamycin, or everolimus.

34. The method of claim 31, where said NsIDIE is an SSRI, a TCA, a phenoxy phenol, an antihistamine, a phenothiazine, or a mu opioid receptor agonist.

35. The method of claim 34, wherein said SSRI is selected from the group consisting of fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram, and escitalopram.

36. The method of claim 34, wherein said TCA is selected from the group consisting of maprotiline, nortriptyline, protriptyline, desipramine, amitriptyline, amoxapine, clomipramine, dothiepin, doxepin, desipramine, imipramine, lofepramine, mianserin, oxaprotiline, octriptyline, and trimipramine.

37. The method of claim 34, wherein said phenoxy phenol is triclosan.

38. The method of claim 34, wherein said antihistamine is selected from the group consisting of desloratadine, thiethylperazine, bromodiphenhydramine, promethazine, cyproheptadine, loratadine, clemizole, azatadine, cetirizine, chlorpheniramine, dimenhydramine, diphenydramine, doxylamine, fexofenadine, meclizine, pyrilamine, and tripelennamine.

39. The method of claim 34, wherein said phenothiazine is chlorpromazine or ethopropazine.

40. The method of claim 34, wherein said mu opioid receptor agonist is loperamide, meperidine, or diphenoxylate.

41. The method of claim 31, wherein said method further comprises administering an NSAID, COX-2 inhibitor, biologic, DMARD, xanthine, anticholinergic compound, beta receptor agonist, bronchodilator, non-steroidal calcineurin inhibitor, vitamin D analog, psoralen, retinoid, or 5-amino salicylic acid.

42. The method of claim 41, wherein said NSAID is ibuprofen, diclofenac, or naproxen.

43. The method of claim 41, wherein said COX-2 inhibitor is rofecoxib, celecoxib, valdecoxib, or lumiracoxib.

44. The method of claim 41, wherein said biologic is adelimumab, etanercept, or infliximab.

45. The method of claim 41, wherein said DMARD is methotrexate or leflunomide.

46. The method of claim 41, wherein said xanthine is theophylline.

47. The method of claim 41, wherein said anticholinergic compound is ipratropium or tiotropium.

48. The method of claim 41, wherein said beta receptor agonist is ibuterol sulfate, bitolterol mesylate, epinephrine, formoterol fumarate, isoproteronol, levalbuterol hydrochloride, metaproterenol sulfate, pirbuterol scetate, salmeterol xinafoate, or terbutaline.

49. The method of claim 41, wherein said vitamin D analog is calcipotriene or calcipotriol.

50. The method of claim 41, wherein said psoralen is methoxsalen.

51. The method of claim 41, wherein said retinoid is acitretin or tazoretene.

52. The method of claim 41, wherein said 5-amino salicylic acid is mesalamine, sulfasalazine, balsalazide disodium, or olsalazine sodium.

53. The method of claim 31, wherein said composition is formulated for topical administration.

54. The method of claim 31, wherein said composition is formulated for systemic administration.

55. A method of decreasing proinflammatory cytokine secretion or production in a cell, said method comprising contacting said cell with an NsIDI and an NsIDIE simultaneously or within 14 days of each other in amounts sufficient *in vivo* to decrease proinflammatory cytokine secretion or production in said cell.

56. The method of claim 55, wherein said cell is a mammalian cell *in vivo*.

57. A kit, comprising:

(i) a composition comprising an NsIDI and an NsIDIE; and

(ii) instructions for administering said composition to a patient diagnosed with or at risk of developing an immunoinflammatory disorder.

58. A kit, comprising:

(i) an NsIDI;

(ii) an NsIDIE; and

(iii) instructions for administering said NsIDI and said NsIDIE to a patient diagnosed with or at risk of developing an immunoinflammatory disorder.

59. A kit comprising:

(i) an NsIDI; and

(ii) instructions for administering said NsIDI and an NsIDIE to a patient diagnosed with or at risk of developing an immunoinflammatory disorder.

60. A kit comprising:

(i) an NsIDIE; and

(ii) instructions for administering said NsIDIE and an NsIDI to a patient diagnosed with or at risk of developing an immunoinflammatory disorder.

61. A method for identifying combinations of compounds useful for suppressing the secretion of proinflammatory cytokines in a patient in need of such treatment, said method comprising the steps of:

(a) contacting cells *in vitro* with an NsIDI and a candidate compound; and

(b) determining whether the combination of said NsIDI and said candidate compound reduces cytokine levels in blood cells stimulated to secrete the cytokines relative to cells contacted with said NsIDI but not contacted with said candidate compound or cells contacted with said candidate compound but not with said NsIDI, wherein a reduction of said cytokine levels identifies said combination as a combination that is useful for treating a patient in need of such treatment.